REMARKS

I. Acknowledgment of Election

Applicants thank the Examiner for acknowledging Applicants' election of Group 1, Claims 1-48, 51, and 52.

II. Replacement Paragraghs Regarding SEQ ID NO:'s

Applicants include replacement paragraphs on page 100 of the originally filed application on page 2 of this paper, and page 116 of the originally filed application on page 2 of this paper, believed consistent with Examiner's request, in light of MPEP Chapter 7, B, which provides:

> Replacement paragraphs must include markings to show the changes. A separate clean version of any replacement paragraphs is not required.

Thus, Applicants include marked-up versions of page 100 and page 116, indicated the appropriate SEQ ID NO:'s. The provided SEQ ID's are consistent with the SEQ ID's submitted in the Preliminary Amended filed April 19, 2004.

For the avoidance of doubt, and confusion, applicants note that page 116 contains two types of underlining. First, certain of the sequence information itself is underlined. This underlining is unchanged from the originally filed application. Second, the text for the various SEQ ID NO:'s has been underlined. This underlining is a modification from the originally filed application, and is the basis for these replacement paragraphs.

III. Replacement Abstract

Applicants also include a replacement abstract, believed to be consistent with MPEP 608.01(b). This replacement abstract is found on page 4 of this paper.

IV. Provisional Nonstatutory Obviousness-type Double Patenting

The Examiner raises a provisional nonstatutory obviousness-type double patenting rejection in view of Claims 1-10 of copending application Aydin (10/666806). Applicants believe this provisional rejection is moot in light of the current claim amendments in the instant case. In any regard, depending on the progression of prosecution in both cases, Applicants are cognizant of the double-patenting issues, as well as the possibility of a terminal disclaimer.

V. Rejection of Claims 1-48 Under 35 U.S.C. §103(a)

The Examiner rejected claims 1-48 under 35 U.S.C. §103 as allegedly being unpatentable over Barany U.S. Patent 6,027,889 (hereafter Barany '889), in view of Wittwer et al., U.S. Patent No. 6,303,305 (hereafter Wittwer). Action at page 7. Applicants respectfully traverse this rejection.

Applicants assert that the Examiner has failed to establish a prima facie case of obviousness. As set forth in the M.P.E.P., the prior art reference (or references when combined) must teach or suggest all the claim limitations. Applicants have amended claim 1. Support for these amendments include elements of various dependant claims, for example claims 2 and 4, as well as

aspects of the embodiment depicted in Figure 10. Thus, neither Barany '889, nor Wittwer, nor the combination of Barany '889 and Wittwer teach or suggest the following, according to Applicants amended claim 1:

A method for detecting the presence or absence of a first target nucleic acid sequence and a second target nucleic acid sequence in a sample comprising:

forming a ligation reaction composition comprising the sample, a first ligation probe set for the first target nucleic acid sequence, and a second ligation probe set for the second target nucleic acid sequence, the first ligation probe set comprising (a) at least one first probe, comprising a target-specific portion and a 5′ primer-specific portion, wherein the 5′ primer-specific portion comprises a sequence, and (b) at least one second probe, comprising a target-specific portion and a 3′ primer-specific portion, wherein the 3′ primer-specific portion comprises a sequence, and the second ligation probe set comprising (a) at least one first probe, comprising a target-specific portion and a 5' primer-specific portion, wherein the 5' primer-specific portion comprises a sequence; wherein the probes in each set are suitable for ligation together when hybridized adjacent to one another on a complementary target sequence, wherein the sequence of the 5′ primer-specific portion of the first probe of the first probe set is different from the sequence of the 5′ primer-specific portion of the first probe of the second probe set, wherein the sequence of the 3' primer-specific portion of the second probe of the first probe set is different from the sequence of the 3' primer-specific portion of the second probe of the second probe, or both the sequence of the 5′ primer-specific portion of the first probe of the first probe set is different from the sequence of the 5′ primer-specific portion of the first probe of the second probe set and the sequence of the 3' primer-specific portion of the second probe of the first probe set is different from the sequence of the 3' primer-specific portion of the second probe of the second probe set, and wherein the first target nucleic acid sequence is different from the second target nucleic acid sequence;

forming a first test composition and a second test composition by subjecting the ligation reaction composition to at least one cycle of ligation, wherein adjacently hybridizing complementary probes of the first ligation probe set are ligated to one another to form a first ligation product comprising the 5′ primer-specific portion, the target-specific portions, and the 3′ primer-specific portion, and wherein adjacently hybridizing complementary probes of the second ligation probe set

are ligated to one another to form a second ligation product comprising the 5' primer-specific portion, the target-specific portion, and the 3' primer-specific portion;

forming a first amplification reaction composition in a first amplification reaction mixture comprising: at least a portion of the first test composition; a polymerase; a double-stranded-dependent specific label, wherein the double-stranded-dependent label has a first detectable signal value when the double-stranded-dependent label is not exposed to double-stranded nucleic acid; a first primer set, the first primer set comprising (i) a first primer comprising the sequence of the 5′ primer-specific portion of the first ligation product, and (ii) a second primer comprising a sequence complementary to the sequence of the 3′ primer-specific portion of the first ligation product;

forming a second amplification reaction composition in a second amplification reaction mixture comprising: a portion of the second test composition; a polymerase; a double-stranded-dependent specific label, wherein the double-stranded-dependent label has a first detectable signal value when the double-stranded-dependent label is not exposed to double-stranded nucleic acid; a second primer set, the second primer set comprising (i) a first primer comprising the sequence of the 5′ primer-specific portion of the second ligation product, and (ii) a second primer comprising a sequence complementary to the sequence of the 3′ primer-specific portion of the second ligation product;

subjecting the first amplification reaction composition to at least one amplification reaction;

subjecting the second amplification reaction composition to at least one amplification reaction;

detecting a second detectable signal value at least one of during and after the at least one first amplification reaction, wherein a threshold difference between the first detectable signal value and the second detectable signal value indicates the presence of the first target nucleic acid sequence, and wherein no threshold difference between the first detectable signal value and the second detectable signal value indicates the absence of the first target nucleic acid sequence; and,

detecting a second detectable signal value at least one of during and after the at least one second amplification reaction, wherein a threshold difference between the first detectable signal value and the second detectable signal value indicates the presence of the second target nucleic acid sequence, and wherein no threshold difference between the first detectable signal value and the second detectable signal value indicates the absence of the second target nucleic acid sequence.

Remaining claims 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, and 26 ultimately depend from claim 1, and thus, also comprise the elements of claim 1. Accordingly, for at least this reason, the combination of Barany '889 and Wittwer, asserted by the Examiner, does not teach or suggest all of the elements of claims 2-48. Therefore, Applicants respectfully assert that the Examiner has not established a prima facie case of obviousness. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-48 under 35 U.S.C. §103(a) as allegedly being unpatentable over Barany '889 in view of Wittwer.

Because claims 1, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, and 26 would not have been obvious for at least the reasons discussed above, Applicants do not need to address the Examiner's contentions concerning other elements of those claims. By not addressing those contentions, Applicants in no way acquiesce to those contentions.

VI. Rejection of Claims 51-52 Under 35 U.S.C. §103(a)

The Examiner rejected claims 51-52 under 35 U.S.C. §103 as allegedly being unpatentable over Barany U.S. Patent 6,027,889 (hereafter Barany '889), in view of Barany et al., U.S. Patent No. 6,312,892 (hereafter Barany '892). Action at page 19. Applicants respectfully traverse this rejection.

Applicants cancel claim 51, thus rendering its rejection moot.

Applicants assert that the Examiner has failed to establish a prima facie case of obviousness. As set forth in the M.P.E.P., the prior art reference (or

references when combined) must teach or suggest all the claim limitations. Applicants have amended claim 51. Support for these amendments include elements of various dependant claims, for example claims 2 and 4, as well as aspects of the embodiment depicted in Figure 10. However, neither Barany '889 nor Barany '892, nor the combination of Barany '889 and Barany '892 teach or suggest the following, according to Applicants amended claim 52:

A method for detecting the presence or absence of a first target nucleic acid sequence and a second target nucleic acid sequence in a sample comprising:

forming a ligation reaction composition comprising the sample, poly-deoxy-inosinic-deoxy-cytidylic acid, a first ligation probe set for the first target nucleic acid sequence, and a second ligation probe set for the second target nucleic acid sequence, the first ligation probe set comprising (a) at least one first probe, comprising a target-specific portion and a 5′ primer-specific portion, wherein the 5′ primer-specific portion comprises a sequence, and (b) at least one second probe, comprising a target-specific portion and a 3′ primer-specific portion, wherein the 3′ primer-specific portion comprises a sequence, and the second ligation probe set comprising (a) at least one first probe, comprising a target-specific portion and a 5' primer-specific portion, wherein the 5' primer-specific portion comprises a sequence; wherein the probes in each set are suitable for ligation together when hybridized adjacent to one another on a complementary target sequence, wherein the sequence of the 5′ primer-specific portion of the first probe of the first probe set is different from the sequence of the 5′ primer-specific portion of the first probe of the second probe set, wherein the sequence of the 3' primer-specific portion of the second probe of the first probe set is different from the sequence of the 3' primer-specific portion of the second probe of the second probe, or both the sequence of the 5′ primer-specific portion of the first probe of the first probe set is different from the sequence of the 5′ primer-specific portion of the first probe of the second probe set and the sequence of the 3' primer-specific portion of the second probe of the first probe set is different from the sequence of the 3' primer-specific portion of the second probe of the second probe set, and wherein the first target nucleic acid sequence is different from the second target nucleic acid sequence;

forming a first test composition and a second test composition by subjecting the ligation reaction composition to at least one cycle of ligation, wherein adjacently hybridizing complementary probes of the first ligation probe set are ligated to one another to form a first ligation product comprising the 5′ primer-specific portion, the target-specific portions, and the 3′ primer-specific

portion, and wherein adjacently hybridizing complementary probes of the second ligation probe set are ligated to one another to form a second ligation product comprising the 5' primer-specific portion, the target-specific portion, and the 3' primer-specific portion;

forming a first amplification reaction composition in a first amplification reaction mixture comprising: at least a portion of the first test composition; a polymerase; and a first primer set, the first primer set comprising (i) a first primer comprising the sequence of the 5′ primer-specific portion of the first ligation product, and (ii) a second primer comprising a sequence complementary to the sequence of the 3′ primer-specific portion of the first ligation product;

forming a second amplification reaction composition in a second amplification reaction mixture comprising: at least a portion of the second test composition; a polymerase; and a second primer set, the second primer set comprising (i) a first primer comprising the sequence of the 5′ primer-specific portion of the second ligation product, and (ii) a second primer comprising a sequence complementary to the sequence of the 3′ primer-specific portion of the second ligation product;

subjecting the first amplification reaction composition to at least one first amplification reaction; and detecting the presence or absence of the first target nucleic acid sequence by detecting whether the at least one first amplification reaction results in amplification product from the first ligation product; and,

subjecting the at least one second amplification reaction composition to at least one second amplification reaction; and detecting the presence or absence of the second target nucleic acid sequence by detecting whether the at least second amplification reaction results in amplification product from the second ligation product.

Accordingly, for at least this reason, the combination of Barany '889 and Barany '892, asserted by the Examiner, does not teach or suggest all of the elements of claims 52. Therefore, Applicants respectfully assert that the Examiner has not established a prima facie case of obviousness. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 52 under 35 U.S.C. §103(a) as allegedly being unpatentable over Barany '889 in view of Barany '892.

Because claim 52 would not have been obvious for at least the reasons discussed above, Applicants do not need to address the Examiner's contentions

concerning other elements of this claim. By not addressing those contentions, Applicants in no way acquiesce to those contentions.

Conclusion

Applicants respectfully request reconsideration of the application and the timely issuance of a Notice of Allowance. In the event that the Examiner does not find the claims allowable, Applicants request that the Examiner contact the undersigned at (650) 554 3392 to set up an interview.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. **01-2213.**

Respectfully submitted,

Date: 7-11-06

Andrew K. Finn
Agent for Applicants
Reg. No. 54.097
Telephone: 650-554-3392
Customer No.: 22896